

PACENA	at C	<u></u>		
	CERT	IFICATE OF MAILING		
I hereby certify that this corresponding Assistant Commissioner for Pate		th the United States Postal Service a	s first class mail i	n an envelope addressed to:
Typed or Printed Name	Steven F.	Goldstein		
Signature	Jt T	Halts	Date	Apr: 11, 2002
		Attorney Docket	23001481	
DECLAR	ATION	First Named Inventor	Williams e	et al.
OF FILIPPO M.	RANDAZZO	Application Number	09/297,64	8
ANI GEORGE F.	=	Filing Date	March 10,	2000
UNDER 37 C.I	•	Group Art Unit	1631	
Address to:	_	Examiner Name	J. Brusca	
Assistant Commissioner for Washington, D.C. 20231	r Patents	Title: Novel Human C	Genes and Ge	ene Expression

Dear Sir:

- I, Filippo M. Randazzo, declare and say I am a resident of the State of California. My residence address is 104 Capricorn Avenue, Oakland, CA 94611.
- 2. I hold a B.S. degree in Molecular Microbiology and Anthropology, which I received from the University of Notre Dame in 1985. I further hold a Ph.D. degree, which I received from Indiana University in 1991. I am skilled in the fields of genetics, molecular biology, developmental biology genomics and cancer biology. I am a co-inventor of the invention claimed in the above-referenced patent application.
- 3. I, George F. Lamson, declare and say I am a resident of the State of California. My residence address is 232 Sandringham Dr., Moraga, CA 94556.
- 4. I hold a BS degree in Biochemistry, which I received from the University of CA, Santa Barbara in 1976. I further hold a PhD degree, which I received from University of CA, Berkeley,

Exhibit 1

in 1982. I am skilled in the fields of Bioinformatics. I am a co-inventor of the invention claimed in the above-referenced patent application.

- 5. I have reviewed the relevant portions of the Office Action (specifically section nos. 6 and 10), mailed October 2, 2001, in the above-referenced application. I understand that claims 58, 60-66, 116, and 126 of the above-referenced patent application are rejected under 35 U.S.C. §101 on the grounds that the claimed invention lacks patentable utility, and also under 35 U.S.C. §112, ¶ 1, on the grounds that since the claimed invention is not supported by a patentable utility, one skilled in the art would not know how to use the claimed invention.
- 6. This Declaration provides further evidence of the patentable utility of the claimed invention. Specifically, this Declaration provides evidence that the nucleotide sequence designated SEQ ID NO: 1186 represents genes that are differentially expressed in cancer cells, thus supporting the assertion that the claimed invention has utility in detecting cancer cells.
- 7. The following experiments were conducted by me or under my direction.
- 8. Genes differentially expressed in cancerous cells were identified as detected by microarray hybridization analysis using materials obtained from patient colon tissue samples. The biological materials used in these experiments, the methods of analysis, and the results are described below.
- 9. Source of patient tissue samples. Normal and cancerous tissues were collected from patients using laser capture microdissection (LCM) techniques, which techniques are well known in the art. Table 1 (Attachment 1) provides information about each patient from which the samples were isolated, including: the Patient ID ("PT ID") and Path ReportID ("Path ID"), which are numbers assigned to the patient and the pathology reports for identification purposes; the group ("Grp") to which the patients have been assigned; the anatomical location of the tumor ("Anatom Loc"); the primary tumor size ("Size"); the primary tumor grade ("Grade"); the identification of

the histopathological grade ("Histo Grade"); a description of local sites to which the tumor had invaded ("Local Invasion"); the presence of lymph node metastases ("Lymph Met"); the incidence of lymph node metastases (provided as a number of lymph nodes positive for metastasis over the number of lymph nodes examined) ("Lymph Met Incid"); the regional lymphnode grade ("Reg Lymph Grade"); the identification or detection of metastases to sites distant to the tumor and their location ("Dist Met & Loc"); the grade of distant metastasis ("Dist Met Grade"); and general comments about the patient or the tumor ("Comments"). Histopathology of all primary tumors indicated the tumor was adenocarcinoma except for Patient ID Nos. 130 (for which no information was provided), 392 (in which greater than 50% of the cells were mucinous carcinoma), and 784 (adenosquamous carcinoma). Extranodal extensions were described in three patients, Patient ID Nos. 784, 789, and 791. Lymphovascular invasion was described in Patient ID Nos. 128, 228, 278, 517, 534, 784, 786, 789, 791, 890, and 892. Crohn's-like infiltrates were described in seven patients, Patient ID Nos. 52, 264, 268, 392, 393, 784, and 791.

- 10. Source of polynucleotides on arrays. Polynucleotides spotted on the arrays were generated by PCR amplification of clones derived from cDNA libraries. The clones used for amplification were either the clones from which the sequences described herein were derived, or are clones having inserts with significant polynucleotide sequence overlap with the sequences described herein as determined by BLAST2 homology searching.
- layout and control spot set. Each microarray was divided into two areas, each area having an array with, on each half, twelve groupings of 32 x 12 spots for a total of about 9,216 spots on each array. The two areas are spotted identically which provide for at least two duplicates of each clone per array. Spotting was accomplished using PCR amplified products from 0.5kb to 2.0 kb and spotted using a Molecular Dynamics Gen III spotter according to the manufacturer's recommendations. The first row of each of the 24 regions on the array had about 32 control spots, including 4 negative control spots and 8 test polynucleotides. The test polynucleotides

3

Exhibit 1

were spiked into each sample before the labeling reaction with a range of concentrations from 2-600 pg/slide and ratios of 1:1. For each array design, two slides were hybridized with the test samples reverse-labeled in the labeling reaction. This provided for about 4 duplicate measurements for each clone, two of one color and two of the other, for each sample.

- 12. Microarray Analysis. cDNA probes were prepared from total RNA isolated from the patient cells described in Table 1 (Attachment 1). Since LCM provides for the isolation of specific cell types to provide a substantially homogenous cell sample, this provided for a similarly pure RNA sample. Total RNA was first reverse transcribed into cDNA using a primer containing a T7 RNA polymerase promoter, followed by second strand DNA synthesis. cDNA was then transcribed in vitro to produce antisense RNA using the T7 promoter-mediated expression, and the antisense RNA was then converted into cDNA. The second set of cDNAs were again transcribed in vitro, using the T7 promoter, to provide antisense RNA. Optionally, the RNA was again converted into cDNA, allowing for up to a third round of T7-mediated amplification to produce more antisense RNA. Thus the procedure provided for two or three rounds of in vitro transcription to produce the final RNA used for fluorescent labeling. Fluorescent probes were generated by first adding control RNA to the antisense RNA mix, and producing fluorescently labeled cDNA from the RNA starting material. Fluorescently labeled cDNAs prepared from the tumor RNA sample were compared to fluorescently labeled cDNAs prepared from normal cell RNA sample. For example, the cDNA probes from the normal cells were labeled with Cy3 fluorescent dye (green) and the cDNA probes prepared from the tumor cells were labeled with Cy5 fluorescent dye (red).
- 13. The differential expression assay was performed by mixing equal amounts of probes from tumor cells and normal cells of the same patient ("matched") or from tumor cells and normal cells of different patients ("unmatched") (i.e., the tumor cells are from one patient and the normal cells are from a different patient). The arrays were prehybridized by incubation for about 2 hrs at 60°C in 5X SSC/0.2% SDS/1 mM EDTA, and then washed three times in water and twice in isopropanol. Following prehybridization of the array, the probe mixture was then hybridized to

the array under conditions of high stringency (overnight at 42°C in 50% formamide, 5X SSC. and 0.2% SDS. After hybridization, the array was washed at 55°C three times as follows: 1) first wash in 1X SSC/0.2% SDS; 2) second wash in 0.1X SSC/0.2% SDS; and 3) third wash in 0.1X SSC. The arrays were then scanned for green and red fluorescence using a Molecular Dynamics Generation III dual color laser-scanner/detector. The images were processed using BioDiscovery Autogene software, and the data from each scan set normalized to provide for a ratio of expression relative to normal. Data from the microarray experiments was analyzed according to the algorithms described in U.S. application serial no. 60/252,358, filed November 20, 2000, by E.J. Moler, M.A. Boyle, and F.M. Randazzo, and entitled "Precision and accuracy in cDNA microarray data." The experiment was repeated, this time labeling the two probes with the opposite color in order to perform the assay in both "color directions." Each experiment was sometimes repeated with two more slides (one in each color direction). The level fluorescence for each sequence on the array expressed as a ratio of the geometric mean of 8 replicate spots/genes from the four arrays or 4 replicate spots/gene from 2 arrays or some other permutation. The data were normalized using the spiked positive controls present in each duplicated area, and the precision of this normalization was included in the final determination of the significance of each differential. The fluorescent intensity of each spot was also compared to the negative controls in each duplicated area to determine which spots detected significant expression levels in each sample.

14. A statistical analysis of the fluorescent intensities was applied to each set of duplicate spots to assess the precision and significance of each differential measurement, resulting in a p-value testing the null hypothesis that there is no differential in the expression level between the tumor and normal samples of each patient. For initial analysis of the microarrays, the hypothesis was accepted if p>10⁻³, and the differential ratio was set to 1.000 for those spots. All other spots have a significant difference in expression between the tumor and normal sample. If the tumor sample has detectable expression and the normal does not, the ratio is truncated at 1000 since the value for expression in the normal sample would be zero, and the ratio would not be a mathematically useful value (e.g., infinity). If the normal sample has detectable expression and

the tumor does not, the ratio is truncated to 0.001, since the value for expression in the tumor sample would be zero and the ratio would not be a mathematically useful value. These latter two situations are referred to herein as "on/off." Database tables were populated using a 95% confidence level (p>0.05).

- In general, a polynucleotide is said to represent a significantly differentially expressed gene between two samples when there is detectable levels of expression in at least one sample and the ratio value is greater than at least about 1.2 fold, preferably greater than at least about 1.5 fold, more preferably greater than at least about 2 fold, where the ratio value is calculated using the method described above. A differential expression ratio of 1 indicates that the expression level of the gene in the tumor cell was not statistically different from expression of that gene in normal colon cells of the same patient. A differential expression ratio significantly greater than 1 in cancerous colon cells relative to normal colon cells indicates that the gene is increased in expression in cancerous cells relative to normal cells, indicating that the gene plays a role in the development of the cancerous phenotype, and may be involved in promoting metastasis of the cell.
- Table 2, shown below, summarizes the results of the differential expression analysis in colon tissue. The table provides: (1) the SEQ ID NO of the polynucleotide corresponding to the polynucleotide on the spot on the array; (2) the Clone Name; (3) whether the tumor cells and normal cells were from the same patient ("matched) or were from different patients ("unmatched"); (4) the number of patients tested ("No. Tested"); (5) the percentage of patients tested in which detected expression level was greater than or equal to a 2-fold increase in cancerous tissue relative to normal tissue (">=2x"); (6) the percentage of patients tested in which detected expression level was greater than or equal to a 5-fold increase in cancerous tissue relative to normal tissue (">=5x"); and (7) the percentage of patients tested in which detected expression level was less than or equal to ½ of the expression level in normal cells ("<=0.5x").

TABLE 2

SEQ ID NO:	Clone Name	Matched/ Unmatched	No. Tested	>=2x 95% conf.	>=5x 95% conf.	<=0.5x 95% conf.
1186	M00032614C:B10	matched	40	67.5	12.5	48.48
1186	M00032614C:B10	unmatched	28	42.9	0.0	3.6

17. The data above support the assertion that a polynucleotide having a sequence of SEQ ID NO: 1186 represents genes that are differentially expressed in cancer cells, thus supporting the assertion that the claimed invention has utility in detecting cancer cells. Specifically, detection of gene products that correspond to genes having a sequence of SEQ ID NO: 1186 can provide an indicator that the cell is cancerous, and may provide a therapeutic and/or diagnostic target.

18. I, Filippo M. Randazzo, hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such will false statements may jeopardize the validity of the application or any patent issuing thereon.

3/28102	a de la companya del companya de la companya del companya de la co
Date	Filippo M. Randazzo

19. I, George Lamson, hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such will false statements may jeopardize the validity of the application or any patent issuing thereon.

3/28/02 Date Darge Lamson

Attachments: Table 1 of patient data

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001481 3	Comment	invasive adenocarcinom a, moderately differentiated; focal perineural invasion is seen	Hyperplastic polyp in appendix.	Perineural invasion; donut anastomosis Neg. One tubulovillous and one tubular adenoma with no high grade dysplasia	patient history of metastatic melanoma	
No.: 23(Dist Met Grade	MX	M0	MO	M0	Mo
Atty Dkt. No.: 23001481 USSN: 09/297,648	Dist Met & Loc	Neg	Neg	Neg	Neg	Neg
	Reg Lymph Grade	ž	0X	0X	0X	Z
	Lymph Met Incid	3/8	0/12	0/34	0/19	1/5
*	Lymph Met	Pos	Neg	Neg	Neg	Pos
Table 1	Local Invasion	Extending into subserosal adipose tissue	Invasion through muscularis propria, subserosal involvement; ileocec. valve involvement	Invasion of muscularis propria into serosa, involving submucosa of urinary bladder	Invasion through the muscularis propria into suserosal adipose tissue. Ileocecal junction.	Invasion of muscularis propria into percolonic fat
	Histo Grade	G2	G3	G2	G2	G 2
	Grade	T3	13	T4	T3	T3
	Siz	4.0	9.0	9	9	5.0
	Anatom Loc	Ascending colon	Cecum	Sigmoid	Cecum	Transverse colon
	Grp		п	п	Ħ	H
Attachment 1	Path ID	21	71	140	441	147
Attach	Pt ID	15	52	121	125	128

Attachment 1

				_					_																				
	001481	<u>~</u>	Comment			Small separate	tubular	adenoma (0.4	cm)					Perineural	invasion	identified	adjacent to	metastatic	adenocarcinom	a.	Separate	tubolovillous	and tubular	adenomas					
	No.: 23(29/,04	Dist Met	M	• !	W0								M1							W0								
	Afty Dkt. No.: 23001481	USSIN: 09/29/,048	Dist Met & Loc	Neg	0	Neg)							Pos -	Liver						Neg								
			Reg Lymph Grade	NZ		9X								N2							Z					-			
	a .		Lymph Met Incid	10/24		6/0								7/21							2/13								
			Lymph Met	Pos		Neg)							Pos							Pos								
	Table 1		Local Invasion	through wall and	into surrounding adipose tissue	Invasion through	muscularis propria	into non-	peritonealized	pericolic tissue;	gross	configuration is	annular.	Invasion of	muscularis propria	into pericolonic	adipose tissue, but	not through serosa.	Arising from	tubular adenoma.	Invasion through	mucsularis propria	ınto	subserosa/pericolic	adipose, no serosal	involvement.	Gross	configuration	annular.
			Histo Grade			G2								G2							25								
			Siz Grade e	T3		T3								T3						į	13								
			Siz	5.5		5.0								5.5						į	 X.								
			Anatom Loc	Splenic	flexure	Rectum								Cecum							Hepatic	Hexare							
		(<u>e</u> 5			П								IV															
,	ment 1		rath 13	149		152			-					160							175								
	Attachment 1		a s	130		133		_						141						į	156								

Atty Dkt. No.: 23001481 USSN: 09/297,648 Table 1

Met Dist Comment	Met	Grade	eg MX Hyperplastic polyps	eg M0 Tubulovillous adenoma with high grade	dysplasia	MX	MX M0	MO MO
Reg Dist Met		Grade	Zeg	N0 Neg	_	Mesenteri c deposit		
	_		Z			Z		
Lymph Lymph.	Met	Incid	1/8	0/10		0/15		
Lymp	Met			Neg		Neg N		
Local Invasion			Invasion through muscularis propria to involve subserosal, perirectoal adipose, and serosa	Invasion through muscularis propria into subserosal adipose tissue.		Invades through muscularis propria to involve pericolonic adipose, extends to serosa.	Invades through muscularis propria to involve pericolonic adipose, extends to serosa. Confined to muscularis propria	Invades through muscularis propria to involve pericolonic adipose, extends to serosa. Confined to muscularis propria Invades full thickness of muscularis propria, but mesenteric adipose free of malignancy
Histo	Grade		G2 to	G2		G2	G2 G2	G G G
Siz Grade			EL	T3		T3	T3	T
Siz	ø		5.8	5.5		6	9 4.5	9 4.5 6.5
Anatom	Loc		Rectum	Ascending colon		Transverse colon	Transverse colon	Transverse colon Ileocecal Cecum
Grp	•			п		H		
Path	e e		247	283		285	285	285 286 287
Pt ID			228	264		266	266	267

Table 1

Atty Dkt. No.: 23001481 USSN: 09/297,648

			_																				_					_				
•	Comment		Melanosis coli	and diverticular	disease.		Inbulovillous	adenoma (2.0	cm) with no	high grade	dysplasia. Neg.	liver biopsy.	1 hyperplastic	polyp identified														Tumor arising	at prior	ileocolic	surgical	anastomosis
250,167	Dist	Met Grade	MO				M0						0W				MX						M0					IW				
USSIN: U9/29 /,048	Dist Met	& Loc	Neg	١			Neg				-		Neg				Neg)					Neg					Pos -	Liver			
	Reg	Lymph Grade	0N			117	Z						0N				NO N						0N					ï				
	Lymph.	Met Incid	0/12			2/13	71/7						9/0				0/4						0/4					1/6				
	Lymph	Met	Neg				ros	į					Neg				Neg						Neg					Pos				
	Local Invasion	•	Invasion through	muscularis propria	into percolic	Transier through	mvasion unrougn	muscularis propria	and invades	pericolic adipose	tissue. Reocecal	Juriculon.	Extends into	perirectal fat but	does not reach	serosa	Invasion through	muscularis propria	to involve	pericolonic fat.	Arising from	villous adenoma.	Through colon	wall into	subserosal adipose	tissue. No serosal	spread seen.	Invasion through	muscularis propria	into subserosal	adipose tissue, not	serosa.
	Histo	Grade	G2			9	5					į	25				G2			•			G2				į	2 5				
	Grade		T3			1	CT										T3										i	T3				
	Siz	ə	5.0			7 7	J.J					- 1	9				7	ш	inv	asi	ve		6.5					7				
	Anatom	Loc	Ascending	colon		m.100)	Cecum						Rectosigmo	p <u>i</u>			Ascending	colon					Sigmoid					Ascending	colon			
	Grp		п			E	III					١	=				П						П					≥				
	Path	A	314			215	CIC						358				360						375					44				
	PtID		295			200	067						339				341						356					392				

Table 1

Atty Dkt. No.: 23001481 USSN: 09/297,648

			_							_		_			$\overline{}$								1				_	_	_				
	Comment									rediagnosis of	oophorectomy	path to	metastatic	colon cancer.	Anatomical	location of	nrimary not	printed inch	notated in	report.	Evidence of	chronic colitis.	No mention of	distant met in	report	•					<u> </u>		
1297,04		Met Grade	ω							M.					M								Mo				Σ	<u> </u>					
USSN: 09/297,648	Dist Met	& Loc	Neg)					-	Pos-	Liver				Pos-	Liver	i	_					Neg				Pos -	Liver					
	Reg	Lymph Grade	2 2					,		8 2					z								N2				22						
	Lymph	Met Incld	0/21							2/0					2/17								9/9				6/12						
*	Lymph	Met	Neg		`					Neg					Pos								Pos				Pos						
	Local Invasion		Cecum, invades	through	muscularis propria	to involve	subserosal adipose	tissue but not	serosa.	Invasive through	muscularis to	involve periserosal	fat; abutting	ileocecal junction.	Invasion through	muscularis propria	involving pericolic	adinose serosal	raipose, serosar	surrace uninvolved			penetrates	muscularis	propria, involves	pericolonic fat.	Invasion through	muscularis propria	extensively	through	submucosal and	extending to	serosa.
	Histo	Grade	G2	_		-			<u> </u>	G2	-	<u></u>			G2								- 25				G2						
	Grade		£I		_					T3					T3					-			T3				T3	•					
	Stz	e	6.0							4.8					7.5								m				5.5						
	Anatom	Гос	Cecum							Cecum													Sigmoid				Ascending	colon					
	Grp		П							ΛI					IV								≥				IV						
	Path	en e	445							465					383								395				595						
	Pt ID		393							413					505								517				546						

Table 1

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Atty Dkt. No.: 23001481

adenosquamous fibrotic, but not invasive poorly differentiated adenocarcinom adenocarcinom polyps present, (% not stated), differentiated diferentiation differentiated adenoma and Comment involved by tumor carcinoma moderately hyperplstic dilated and moderately Appendix mucinous invasive tubular a with USSN: 09/297,648 Grade Dist Met ğ MX MI ¥ Dist Met & Loc Pos -Liver Neg Neg Pos -Liver Reg Lymph Grade ž 2 2 Z 2 Lymph Lymph Incid 0/58 Met 0/12 0/22 5/17 Neg Met Neg Pos Neg muscularis propria muscularis propria extending through Local Invasion into pericolic soft into pericolic fat, Invasion through adipose. Serosal but not at serosal bowel wall into the bowel wall, surface free of into suberosal serosal fat through tissues through surface tumor. Grade Siz Grade Histo G2 G2 G5 3 **T**3 13 **T**3 T3 11. 5 3.5 9.5 4.0 Ð Descending colon Ascending colon Anatom Loc Cecum Cecum Grp \geq 2 ш Path 969 714 803 805 8 Pt ID 577 695 784 786

Attach	Attachment 1						Table 1				Atty Dkt. No.: 23001481 USSN: 09/297,648	No.: 23(/297,648	01481
Pt ID	Pt ID Path ID	Grp	Anatom Loc	Siz	Siz Grade Histo e Grade	Histo Grade	Local Invasion Lymph Lymph Met Met Incid	Lymph Met	Lymph Met Incid	Reg Lymph Grade	Dist Met Dist & Loc Met Grad	Dist Met Grade	Сошш
787	806	п	Rectosigmo 2.5	2.5	T3	G2-G3	T3 G2-G3 Invasion of muscularis propria into soft tissue	Neg		0 X	Neg	MX	Peritumor lymphocy response; examined pericolic functional metastatas observed.
789	808	IV	Cecum	5.0	Т3	G2-G3	T3 G2-G3 Extending through muscularis propria into pericolonic fat	Pos	5/10	NZ	Pos - Liver	M	Three fung lesions examined
790	809	ΛI	Rectum	8.9	T3	G1-G2	T3 G1-G2 Invading through	Pos	3/13	ź	Poe	Ž	

								<u>_</u> _													'							_				
Comment			lymphocytic	response; 5 LN	examined in	pericolic fat, no	metastatases	observed.	Three fungating	lesions	examined.				poorly	differentiated	invasive	colonic	adenocarcinom	а	portal lymph	node biopsy	shows poorly	differentiated	metastatic	adenocarcinom	a consistent	מ כטווסופוכווו	with colonic	primary tumor		
Dist	Met Grade	ΧX							M			Ψ			MI						Ē		_								M1	Σ
Dist Met	& Loc	Neg							Pos-	Liver		Pos-	Liver		Pos -	Liver					Pos-liver			_			_	_			Pos-liver, 3 foci	Pos-liver
	Lymph Grade	0X		_	_				N2	_		ź			N2			_							_	_		_				
Lymph	Met Incid			_					5/10			3/13			13/25	_	_	_	_		1/1	_				_		_				
Lymph Lymph	Met	Neg					_		Pos			Pos			Pos						Pos	_	_		_	_	_	_			Neg	Neg
Local Invasion			muscularis propria	into soft tissue						muscularis propria	into pericolonic fat	G1-G2 Invading through	muscularis propria	into perirectal fat	Through the	muscularis propria	into pericolic fat											_				
Histo	Grade	G2-G3		_	_	_			G2-G3			G1-G2		- 1	ප ප						3							_				
Siz Grade Histo		LI	_		_		_		IJ	_		ET	_	⊥	<u> </u>						_	_		_				_	_			
SIZ	ө	2.5	_	_	_	_	_		5.0	_		6.8	_	ٳؙ	5.8	_		_	_			_	_	_	_	_	_	_	_			
Anatom	Loc	Rectosigmo	10						Cecum			Rectum			Ascending	colon												_				
<u>e</u>		ш							2			≥			≥	_					≥							_			≥.	IV
_	A	908		_	_				808			608			810						820		_	_	_	_		_			821	823
F. I.D.		787							789			790		1	791						801									200	802	804

Table 1

Atty Dkt. No.: 23001481 USSN: 09/297,648

	_		_	$\overline{}$			_	_	_			_	_			_	_			_	_	_	-	_	_			_	
	Comment			celiac lymph	node biopsy	shows	metastatic	adenocarcinom	a consistent	with colonic	primary tumor																		
040,127	Dist	Met	Grade	M1								Ξ	M	Ξ	Σ	Σ	Σ			Ž	M	Σ	Σ	M	M			MI	Σ
USSIN: 07/27/,040	Dist Met	& Loc		Pos-liver								Pos-liver	Pos-liver	Pos-liver	Pos-liver	Pos-liver	Pos-liver			Pos-liver	Pos-liver	Pos-liver	Pos-liver	Pos-liver	Pos-liver,	duodenu	ш	Pos-liver	Pos-liver
	Reg	Lymph	Grade														N2												
	Lymph	Met	Incid	1,1													111												
	Lymph	Met		Pos								Neg	Neg	Neg	Neg	Neg	Pos			Neg	Neg	Neg	Neg	Neg	Neg			Neg	Neg
	Local Invasion																through	muscularis propria	into pericolonic soft tissue										
	Histo	Grade								••		3					G2					G2	G2						G 2
	Siz Grade																£L												
į	Siz	e e															3.0												
	Anatom	Loc															Sigmoid												
ľ	5			≥								2	≥	2	2	2	2			Σ	2	2	2	≥	≥			≥	2
	Path	9		824								825	826	827	828	830	832			833	834	836	837	838	839			840	841
	m za			802]	908	807	808	809	811	813			814	815	817	818	819	820			821	822

Table 1

Atty Dkt. No.: 23001481 USSN: 09/297,648

	Comment		moderately to	poorly	differentiated	primary tumor										moderately to	poorly	differentiated	moderately to	poorly	differentiated	metastatic	tumor							
10,10	Dist	Met Grade	Ξ				MI					M			M	MI			Mi					Mi	MI	MI	Ē	M		M
USSIN: US/29/,040	Dist Met	& Loc	Pos-liver				Pos-liver,	diaphrag	Ë,	gallbladd	er nodule	Pos-liver,	peritonen	ш	Pos-liver	Pos-liver			Pos-liver					Pos-liver						
	Reg	Lymph Grade	īz							-																			*	
		Met Incid	2/11																						2/2					
	Lymph	Met	Pos				Neg			,-		Neg			Neg	Neg			Neg			,		Neg	Pos	Neg	Neg	Neg	Neg	Neg
	Local Invasion		through	muscularis propria	into perirectal soft	tissue																								
	Histo	Grade	C3																G3				5	3		G2			G2	G2
	Siz Grade		T3																			-								
	Siz	e	5.0							9													Ţ							
	Anatom	Loc	Descending	colon																										
	Grb		2				≥					≥			≥	≥			2				È	<u> </u>	2	≥	≥	2		2
	Path	9	842				845					846			847	848			849				050	000	851	852	853	854	855	856
	Pt ID		823				826					827			828	829			830				1,60	100	832	833	834	835	836	837

e1	
Table	
nt 1	
Attachmen	

Atty Dkt. No.: 23001481

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Patient with a history of colon adenocarcinom a adenocarcinom as; this patient moderately differentiated sigmoid colon has tumors of the ascending differentiated colon and the Comment Perineural invasion moderately extensive. Perineural invasion present. present, well to cancer. USSN: 09/297,648 Grade Met Ξ Ξ Dist Met Dist M Z Ξ Liver, left omentum and right & Loc Poslobe, Pos-Liver Pos -Liver Pos -Liver Pos -Liver Reg Lymph Grade 2 2 N2 N Z Z Lymph Lymph Incid 11/15 Met 4/15 1/28 3/21 1/4 Met Pos Pos Pos Pos Pos muscularis propria into perirectal soft muscularis propria muscularis propria Local Invasion Invasion through attached to colon. focally invading skeletal muscle Into muscularis into subserosa. tissue. Tumor pericolic sort int subserosal Invasion into Through Through propria tissue tissue Grade Siz Grade Histo G2 G G2 G2 G2 T2**T**3 끄 T3 **T**3 5.2 5.0 2.0 4.8 a) Ascending Ascending Anatom Loc Sigmoid Rectum Cecum colon colon Grb \sim ≥ 2 ≥ 2 Path 806 606 910 912 911 8 Pt ID 888 688 890 891 892

Atty Dkt. No.: 23001481 USSN: 09/297,648	Comment	Perineural invasion focally present. Omentum mass, but resection with no tumor
	Dist Met	MI
	Dist Met & Loc	Pos - Liver
	ymph Reg Met Lymph Incid Grade	NZ
	Lymph Met Incid	14/17
	Lymph Met	Pos
Table 1	Siz Grade Histo Local Invasion Lymph Lymph Reg Dist Met Dist e Grade Grade Grade Grade Grade Grade	6.0 T3 G2-G3 Through muscularis propria into pericolic fat
	Histo Grade	G2-G3
	Grade	ET
	Siz e	0.9
ment 1	Anatom Loc	Transverse colon
	Grp	2
	Pt ID Path Grp ID	913
Attachment 1	Pt ID	



NCB1

Entrez

BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]

Match: 0 Mismatch: 0 gap open: 11 gap extension: 1	
x_dropoff: 50 expect: 10.0000 wordsize: 3 Filter Align	
Sequence lcl seq_1	Length 299 (1 299)
vd20e09.s1 Knowles Solter mouse 2 cell Mus musculus Sequence gi cDNA clone IMAGE:793096 5' similar to TR:G555806 2 2156932 G555806 4-HYDROXYPHENYLPYRUVATE ACID DIOXYGENASE.;.	Length 415 (1 415)
2	
NOTE: The statistics (bitscore and expect value) is calculated based on the size of	nr database
Score = 104 bits (222), Expect = 2e-21 Identities = 39/50 (78%) Frame = +1 / +3	
Query: 4 LTLACTPGSSPTLLRWFHDCLGFCHLPLSPGEDPELGLEMTAGFGLGGMR 153 LTLACT GSSP L+RWFHDCLGF HLPLSPGEDPE+GL++ AG G GG+R Sbjct: 3 LTLACTSGSSPMLMRWFHDCLGFHHLPLSPGEDPEMGLKVAAGSGRGGLR 152	11
Score = 93.2 bits (197), Expect = 6e-18 Identities = 37/48 (77%) Frame = -1 / -1	

Sbjct: 145 PPRPDPAATLRPISGSSPGLSGKW*KPRQSWNQRISIGELPEVQAKVK 2

Blast Result Page 2 of 3

```
Score = 84.5 bits (178), Expect = 3e-15
Identities = 35/48 (72%)
 Frame = -3 / -3
Query: 147 SPKPKPCCHFKAQLGIFTWAQRQVAKAQAVVEPAQKCGGAAGGAGQGQ 4
           SP P+PC H +A L I TWAQRQV KA AVVEPA K GAAGGAGQGQ
                                                                10
Sbjct: 146 SPSPRPCSHLEAHLRILTWAQRQVVKA*AVVEPAHKHRGAAGGAGQGQ 3
Score = 81.7 bits (172), Expect = 2e-14
Identities = 35/49 (71%)
 Frame = +2 / +1
           T*PWPAPPAAPPHFCAGSTTAWAFATCR*AQVKIPSWALK*QQGLGLGE 148
Query: 2
           T*PWPAPPAAP
                        CAGSTTA AF TCR*AQV+I WA + QGLG G+
           T*PWPAPPAAPLCLCAGSTTA*AFTTCR*AQVRIRRWASRWLQGLGEGD 147
Sbjct: 1
Score = 73.9 bits (155), Expect = 4e-12
Identities = 33/47 (70%)
 Frame = +3 / +2
Query: 6
          DLGLHPRQLPHTFALVPRLPGLLPLAAEPR*RSRAGP*NDSRVWAWG 146
          DLGLH RQLP+ +ALVPRLP L PLAAEPR* S GP
                                                    RVWA G
          DLGLHLRQLPYAYALVPRLPRLSPLAAEPR*GSGDGPQGGCRVWARG 145
Sbjct: 5
Score = 70.3 bits (147), Expect = 5e-11
Identities = 33/47 (70%)
 Frame = -2 / -2
Query: 145 PQAQTLLSFQGPARDLHLGSAASGKSPGSRGTSAKVWGSCRGCRPRS 5
                    GP+ D HLGSAASG+S GSRGTSA
           P AQTL
Sbjct: 144 PLAQTLQPP*GPSPDPHLGSAASGESLGSRGTSA*A*GSCRRCRPRS 4
CPU time:
              0.07 user secs.
                                    0.03 sys. secs
                                                             0.10 total secs.
Lambda
           K
            0.135
                     0.401
   0.318
Matrix: BLOSUM62
Number of Hits to DB: 623
Number of Sequences: 0
Number of extensions: 18
Number of successful extensions: 6
Number of sequences better than 10.0: 1
length of database: 1,668,972,645
effective HSP length: 54
effective length of database: 1,367,552,853
effective search space used: 61539878385
frameshift window, decay const: 50, 0.1
T: 13
```

A: 40 X1: 16 (7.3 bits) X2: 109 (49.9 bits) S1: 41 (21.7 bits)



Blast 2 Sequences results

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BLAST

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Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]

Match:	Mismatch: 0 gap open:	gap extension:	
x_dropoff:	50 expect: 10.0000 wordsiz	e: 3 Filter Align	
Sequence 1			Length 300 (1 300)
Sequence 2	gi cDNA clone IMAG	fetal_heart_NbHH19W Homo sapiens E:346656 5' similar to contains Alu ontains element TAR1 repetitive	Length 446 (1 446)
		2	
		1	

NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score = 70.7 bits (148), Expect(2) = 2e-18
Identities = 28/29 (96%)
Frame = -1 / -2
```

Page 2 of 4

```
Query: 216 SAHRNLHLLKGF*WQNVSLNAGPRITAPA 130
           SAHRNLHLLKGF*WQN+SLNAGPRITAPA
Sbjct: 445 SAHRNLHLLKGF*WQNLSLNAGPRITAPA 359
Score = 70.3 bits (147), Expect = 5e-11
Identities = 32/47 (68%)
 Frame = +1 / +2
Query: 76 RHEPPRLAKGFNELMDVQCWGCYSRACIETHILPSKAF*EVEVAVS* 216
                                                                   12
                             CWGCYSRACIET ILPSKAF*EVEVAVS*
           RHE
                   K
Sbjct: 305 RHEHHAWPKDLMN*WMYSCWGCYSRACIETQILPSKAF*EVEVAVS* 445
Score = 70.3 bits (147), Expect(2) = 1e-18
Identities = 28/29 (96%)
 Frame = +2 / +3
Query: 131 AGAVILGPALRLTFCHQKPFKRWRLR*AD 217
                                                  13
           AGAVILGPALRL FCHOKPFKRWRLR*AD
Sbjct: 360 AGAVILGPALRLKFCHQKPFKRWRLR*AD 446
Score = 68.0 bits (142), Expect(2) = 2e-16
Identities = 28/29 (96%)
 Frame = -3 / -1
Query: 217 VSSPQPPPLKRLLMAKCESQCRP*NNSPS 131
           VSSPOPPPLKRLLMAK ESOCRP*NNSPS
                                                  16
Sbjct: 446 VSSPQPPPLKRLLMAKFESQCRP*NNSPS 360
Score = 64.3 bits (134), Expect(2) = 2e-15
Identities = 27/29 (93%)
 Frame = +3 / +1
Query: 129 VLGLLF*GLH*DSHFAIKSLLRGGGCGEL 215
                                                  15
           +LGLLF*GLH*DS+FAIKSLLRGGGCGEL
Sbjct: 358 LLGLLF*GLH*DSNFAIKSLLRGGGCGEL 444
Score = 57.9 bits (120), Expect(2) = 1e-12
Identities = 27/28 (96%)
 Frame = -2 / -3
Query: 215 QLTATSTS*KAFDGKM*VSMQALE*QPQ 132
           QLTATSTS*KAFDGK+*VSMQALE*QPQ
Sbjct: 444 QLTATSTS*KAFDGKI*VSMQALE*QPQ 361
Score = 45.0 bits (92), Expect(2) = 1e-18
Identities = 15/15 (100%)
 Frame = +2 / +2
```

Page 3 of 4

```
Query: 86 HHAWPKDLMN*WMYS 130
          HHAWPKDLMN*WMYS
Sbjct: 314 HHAWPKDLMN*WMYS 358
Score = 44.1 bits (90), Expect(2) = 2e-18
Identities = 16/18 (88%)
 Frame = -3 / -2
Query: 139 SPSTVHPLIH*ILWPGVV 86
           +P+TVHPLIH*ILWPGVV
Sbjct: 367 APATVHPLIH*ILWPGVV 314
Score = 40.0 bits (81), Expect(2) = 2e-16
Identities = 15/17 (88%)
Frame = -2 / -1
Query: 137 PQHCTSINSLNPLARRG 87
           P +CTSINSLNPLARRG
Sbjct: 365 PSNCTSINSLNPLARRG 315
Score = 40.0 bits (81), Expect (2) = 2e-15
Identities = 17/23 (73%)
Frame = +3 / +3
Query: 84 ATTPGQRI**INGCTVLGLLF*G 152
          +TTPGQRI**INGCTV G + G
Sbjct: 312 STTPGQRI**INGCTVAGAVILG 380
Score = 37.3 bits (75), Expect(2) = 1e-12
Identities = 14/14 (100%)
 Frame = -1 / -3
Query: 129 LYIH*FIKSFGQAW 88
           LYIH*FIKSFGQAW
Sbjct: 357 LYIH*FIKSFGQAW 316
Score = 37.3 bits (75), Expect = 0.42
Identities = 15/17 (88%)
 Frame = +1 / +1
Query: 88 PRLAKGFNELMDVQCWG 138
                                     14
           PRLAKGFNELMDVQ G
```

Sbjct: 316 PRLAKGFNELMDVQLLG 366

'Blast Result Page 4 of 4

CPU time: 0.09 user secs. 0.02 sys. secs 0.11 total secs.

Lambda K H 0.318 0.135 0.401

Matrix: BLOSUM62

Number of Hits to DB: 581 Number of Sequences: 0 Number of extensions: 24

Number of successful extensions: 12 Number of sequences better than 10.0: 1

length of database: 1,668,972,645

effective HSP length: 54

effective length of database: 1,368,557,577 effective search space used: 61585090965 frameshift window, decay const: 50, 0.1

T: 13 A: 40

X1: 16 (7.3 bits) X2: 109 (49.9 bits) S1: 41 (21.7 bits)



Blast 2 Sequences results

PubMed

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BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]

Match:0	Mismato	:h:0	gap open:	gap ex	tension:	1		
x_dropoff:	50 expe	ect: 10.000	wordsize	³ Filt	er 🔽	Align		
Sequence 1	lcl seq_1					·		Length 300 (1 300)
Sequence 2	gi 1375806		orl Soares or cDNA clo				5 Mus	Length 342 (1 342)
		<u> </u>			2			
		_						
		<u>_</u>						
	_							
	_ _							
								
A					a se			
					F			
		<u> </u>						
		<u> </u>		•				
		<u> </u>						1
								1

NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score = 174 bits (375), Expect(2) = 1e-47

Identities = 69/82 (84%)

Frame = +2 / +2
```

Query: 53 LRSLTRQLVQDENVRGVITMNEEYETRFLCNSSQEWKRLGVEQLRLSTVDMTGIPTLDNL 232 L+++TR+LV DENVRGVITMNEEYETRFLCN+S+EWK+ GVEQLRLSTVDMTG+PTL NL

21

```
Sbjct: 68 LKNMTRRLVLDENVRGVITMNEEYETRFLCNTSKEWKKAGVEQLRLSTVDMTGVPTLANL 247
Query: 233 QKGVQFALKYQSLGQCVYVHCK 298
            KGVQFALKYQ+LGQCVYVHCK
Sbjct: 248 HKGVQFALKYQALGQCVYVHCK 313
Score = 166 \text{ bits } (356), \text{ Expect}(2) = 6e-42
Identities = 67/79 (84%)
 Frame = -1 / -1
Query: 300 ALQCT*THWPSDWYLRANWTPFWRLSKVGIPVMSTVLSRSCSTPSLFHSCEELHRNLVSY 121
           ALQCT*THWPS WYLRANWTP WRL+KVG PVMSTVLSRSCSTP+ FHS E LHRN VSY
Sbjct: 315 ALQCT*THWPSAWYLRANWTPLWRLAKVGTPVMSTVLSRSCSTPAFFHSFEVLHRNRVSY 136
Query: 120 SSFMVITPRTFSSCTSWRV 64
           SSF+VITPRTFSS TS RV
Sbjct: 135 SSFIVITPRTFSSSTSRRV 79
Score = 146 \text{ bits } (313), \text{ Expect } (2) = 4e-38
Identities = 59/87 (67%)
 Frame = +1 / +1
Query: 40 GALRVAELDAPAGTGRERARGDHHERGVRDEVPVQLFTGVEETRSRXXXXQHSRHDWDPH 219
                 E DAPAGTGRERARGDH+ERGVRD +PVQ
                                                 G+EE+RS
                                                              QHSRHDW P+
           GRAAAEEHDAPAGTGRERARGDHYERGVRDPIPVQHLEGMEESRS*AATAQHSRHDWGPN 234
Query: 220 LGQPPEGSPICSQVPVAGPVCLRAL*G 300
           LGQ P+ SP+CSQVP GPVCL AL*G
Sbjct: 235 LGQSPQRSPVCSQVPGTGPVCLCAL*G 315
Score = 90.4 bits (191), Expect = 4e-17
Identities = 40/75 (53%)
 Frame = +3 / +3
Query: 75
          WYRTRTCAXXXXXXXXXXXXCATLHRSGRD*ESXXXXSAQ*T*LGSPPWTTSRRESNLL 254
                                CAT R+GR E
                                                  SAQ T*LGS PW S +ES+LL
Sbjct: 90 WYWTRTCAG*SL*TRSTRPDSCATPRRNGRKQELSSYGSAQST*LGSQPWPISTKESSLL 269
Query: 255 SSTSRWASVFTCIVR 299
           SST WASV CIVR
Sbjct: 270 SSTRHWASVSMCIVR 314
Score = 70.3 bits (147), Expect(3) = 5e-21
Identities = 28/38 (73%)
 Frame = -3 / -3
```

Query: 298 LTMHVNTLAQRLVLESKLDSLLEVVQGGDPSHVYCAEX 185

```
LTMH++TLAQ LVLESKLDS +E+ QG DPSHV CAE
Sbjct: 313 LTMHIDTLAQCLVLESKLDSFVEIGQGWDPSHVDCAEP 200
Score = 60.2 bits (125), Expect(2) = 7e-09
Identities = 33/55 (60%)
 Frame = -2 / -2
Query: 299 PYNARKHTGPATGT*EQIGLPSGGCPRWGSQSXXXXXXXXXXXXLVSSTPVKSCTG 135
           PYNA +HTGP GT*EQ GL G PR G QS
                                                     L+SS P + CTG
Sbjct: 314 PYNAHRHTGPVPGT*EQTGLLCGDWPRLGPQSCRLC*AVAAQLLLSSIPSRCCTG 150
Score = 47.8 bits (98), Expect(3) = 5e-21
Identities = 10/24 (41%)
 Frame = -3 / -3
Query: 145 VAQXXXXXXXXXXXXXAHVLVLYQ 74
           VAQ
Sbjct: 160 VAQESGLVLLVHSDHPAHVLVQYQ 89
Score = 37.7 bits (76), Expect(2) = 1e-47
Identities = 2/15 (13%)
 Frame = +1 / +2
Query: 4 DWXXXXXXXXXXXX 48
Sbjct: 20 DWYHRIDHTVLLGAL 64
Score = 34.1 bits (68), Expect(2) = 4e-38
Identities = 2/19 (10%)
 Frame = +2 / +3
Query: 5 TGXXXXXXXXXXXXXXX 61
          TG
Sbjct: 21 TGTTASTTRFCWARCR*RT 77
Score = 27.2 bits (53), Expect(2) = 6e-42
Identities = 2/15 (13%)
 Frame = -1 / -3
Query: 48 XXXXXXXXXXXXVV 4
Sbjct: 64 QRAQQNRVVDAVVPV 20
Score = 22.6 bits (43), Expect(3) = 5e-21
Identities = 3/9 (33%)
 Frame = -2 / -1
```

```
Query: 29 XXXXXXYQS 3
YQS
Sbjct: 45 VWSMRWYQS 19
Score = 21.7 bits (41), Expect(2) = 7e-09
Identities = 2/7 (28%)
Frame = -3 / -2
```

Query: 25 XXXXXTS 5 TS Sbjct: 41 GRCGGTS 21

CPU time: 0.10 user secs.

0.03 sys. secs

0.13 total secs.

Lambda K H

S1: 41 (21.7 bits)

0.318 0.135 0.401

Matrix: BLOSUM62
Number of Hits to DB: 662
Number of Sequences: 0
Number of extensions: 21
Number of successful extensions: 12
Number of sequences better than 10.0: 1
length of database: 1,720,680,694
effective HSP length: 54
effective length of database: 1,410,958,186
effective search space used: 63493118370
frameshift window, decay const: 50, 0.1
T: 13
A: 40
X1: 16 (7.3 bits)
X2: 109 (49.9 bits)

Exhibit 5 SEQ ID 1186



Blast 2 Sequences results

PubMed

Entrez

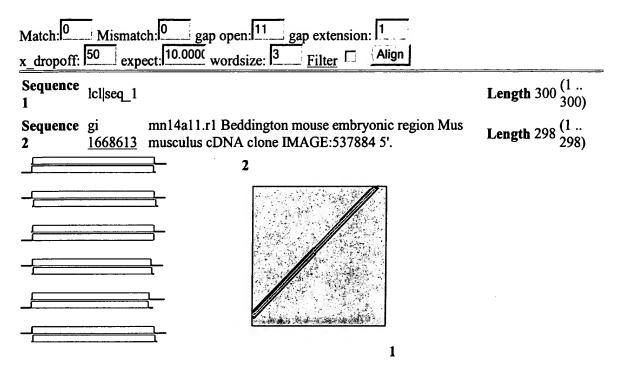
BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]



NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score = 220 bits (474), Expect = 4e-56

Identities = 91/91 (100%)

Frame = +3 / +3
```

Query: 3 DLCRESDLRHAMANCFEALIGAVYLEGSLEEAKQLFGRLLFNDPDLREVWLNYPLHPLQL 182 DLCRESDLRHAMANCFEALIGAVYLEGSLEEAKQLFGRLLFNDPDLREVWLNYPLHPLQL Sbjct: 24 DLCRESDLRHAMANCFEALIGAVYLEGSLEEAKQLFGRLLFNDPDLREVWLNYPLHPLQL 203

91

```
Query: 183 QEPNTDRQLIETSPVLQKLTEFEEAIGVIFT 275
QEPNTDRQLIETSPVLQKLTEFEEAIGVIFT
Sbjct: 204 QEPNTDRQLIETSPVLQKLTEFEEAIGVIFT 296

Score = 202 bits (435), Expect = 9e-51
Identities = 89/92 (96%)
Frame = -3 / -1
```

Query: 277 *VKITPIASSNSVSFCRTGEVSISCRSVFGSCSWSGWRG*LSQTSRRSGSLKSKRPNNCL 98 *VKITPIASSNSVSFCRTGEVSISCRSVFGSCSWSGWRG*LSQTSRRSGSLKSKRPNNCL

Blast Result Page 2 of 3

```
Sbjct: 298 *VKITPIASSNSVSFCRTGEVSISCRSVFGSCSWSGWRG*LSQTSRRSGSLKSKRPNNCL 119
Query: 97 ASSRLPSK*TAPINASKQLAIACRRSDSLQRS 2
           ASSRLPSK*TAPI ASKQLAIA RRSDSL RS
Sbjct: 118 ASSRLPSK*TAPIKASKQLAIAWRRSDSLHRS 23
Score = 157 bits (337), Expect = 3e-37
Identities = 69/91 (75%)
 Frame = +2 / +2
Query: 5
           PL*RIGPSTCNGOLF*SVNRSCLLGGKPGGSOAVIWTLAL**SGPARSLAQLSSPPTPTT 184
                   C+GQLF*S++RSCLLGG+P GSQ VIWTL L**SGP+RSLAQLSSPPTPTT
           P+*RI
Sbjct: 26 PM*RIRSPPCDGQLF*SLDRSCLLGGEPRGSQTVIWTLTL**SGPSRSLAQLSSPPTPTT 205
Query: 185 RAKY*STTY*NFSSSTKTY*V*RSNWSNFYS 277
           RAKY S TY*NF SST+TY V*RS+WS+ +S
Sbjct: 206 RAKYGSATY*NFPSSTETYGV*RSDWSDLHS 298
Score = 149 bits (321), Expect = 5e-35
Identities = 68/89 (76%)
 Frame = -2 / -3
Query: 275 SKNYSNCFFKLSKFL*NWRSFNKLSISIWLL*LEWVERIIEPDFAQVRIIKEQASK*LLG 96
           S+++SN FFKL KFL*NW SFNKL I IWLL*LEWVERIIEPDF++VRIIKE ASK*L G
Sbjct: 296 SEDHSNRFFKLRKFL*NWGSFNKLPIRIWLL*LEWVERIIEPDFSKVRIIKE*ASK*LFG 117
Query: 95
          FLQASLQVNSSY*RFKTIGHCMSKVRFST 9
           FL A LQVNSSY FKTIGH M+++ FST
Sbjct: 116 FL*APLQVNSSYQGFKTIGHRMAEI*FST 30
Score = 149 bits (320), Expect = 7e-35
Identities = 69/88 (78%)
 Frame = +1 / +1
Query: 4
           TFVENRTFDMQWPIVLKR**ELFTWREAWRKPSSYLDACSLMIRTCAKSGSIILSTHSNY 183
                   M+WPIVLK **ELFTWR A RKP+SYLDA SLMIRT KSGSIILSTHSNY
Sbjct: 25 TYVENQISAMRWPIVLKP**ELFTWRGA*RKPNSYLDAYSLMIRTFEKSGSIILSTHSNY 204
Query: 184 KSQILIDNLLKLLQFYKNLLSLKKQLE* 267
           KSQI I NLLKL QFY+NL SLKK+LE*
Sbjct: 205 KSQIRIGNLLKLPQFYRNLRSLKKRLE* 288
Score = 146 bits (313), Expect = 6e-34
Identities = 69/92 (75%)
 Frame = -1 / -2
```

Query: 276 E*KLLQLLLQTQ*VFVELEKFQ*VVDQYLALVVGVGGEDN*ARLRAGPDH*RASVQITAW 97

Blast Result Page 3 of 3

E*+ LQ LLQT *V VEL KFQ*V D YLALVVGVGGEDN*ARL GPDH*R SVQIT W Sbjct: 297 E*RSLQSLLQTP*VSVELGKFQ*VADPYLALVVGVGGEDN*ARLLEGPDH*RVSVQITVW 118

Query: 96 LPPGFPPSKQLLLTLQNNWPLHVEGPILYKGQ 1

LP G PPSKQLL LQNNWP H ILY G+ Sbjct: 117 LPLGSPPSKQLLSRLQNNWPSHGGDLILYIGR 22

CPU time: 0.05 user secs. 0.06 sys. secs 0.11 total secs.

Lambda K

0.318 0.135 0.401

Matrix: BLOSUM62

Number of Hits to DB: 638 Number of Sequences: 0 Number of extensions: 19

Number of successful extensions: 6 Number of sequences better than 10.0: 1

length of database: 1,668,972,645

effective HSP length: 54

effective length of database: 1,368,557,577 effective search space used: 61585090965 frameshift window, decay const: 50, 0.1 T: 13 A: 40

X1: 16 (7.3 bits) X2: 109 (49.9 bits) S1: 41 (21.7 bits)



Blast 2 Sequences results

PubMed

Entrez

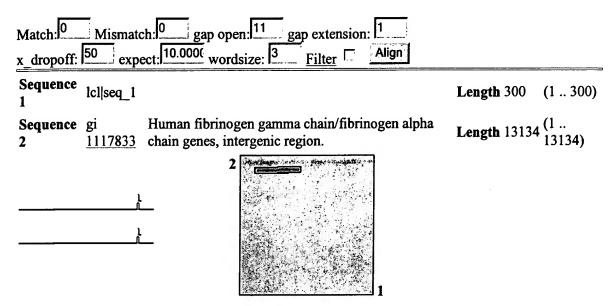
BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]



NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

CPU time:

0.06 user secs.

0.03 sys. secs

0.09 total secs.

Lambda K H 0.318 0.135 0.401

Matrix: BLOSUM62

Page 2 of 2

Number of Hits to DB: 11,835
Number of Sequences: 0
Number of extensions: 205
Number of successful extensions: 10
Number of sequences better than 10.0: 1
length of database: 1,668,972,645
effective HSP length: 54
effective length of database: 1,368,557,577
effective search space used: 61585090965
frameshift window, decay const: 50, 0.1
T: 13
A: 40
X1: 16 (7.3 bits)
X2: 109 (49.9 bits)
S1: 41 (21.7 bits)



Blast 2 Sequences results

PubMed

Entrez

BLAST

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Taxonomy

Structure :

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]

Match: 0 x_dropoff:	Mismatch: gap open: 11 gap extens	sion: 1 Align	
Sequence 1	lcl seq_1	,	Length 209 (1 209)
Sequence 2	gi Human XP1PO ribosomal protein 555940 complete cds.	S3 (rpS3) mRNA,	Length 754 (1 754)
	2		
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2			
8			
		1 -	

NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score = 108 bits (231), Expect = 5e-23
Identities = 44/69 (63%)
Frame = -3 / -3
```

Query: 207 RRTCYAVGTGWGMAEGSGFPPFCSEMGVVGSISSMGSTMMPWDPTGNRGPKKPLPDHVSI 28 RR CYAVGTGWGMA GSGFPPFCSEMGVVGSISS+GSTM+ W G GP P+ S+

Page 2 of 4

Blast Result

```
Sbjct: 743 RRPCYAVGTGWGMAGGSGFPPFCSEMGVVGSISSLGSTMLTWSGRGFLGPILPVGSQGSM 564
Query: 27 VVRLALRSP 1
           + L +P
Sbjct: 563 IFTLMPSTP 537
Score = 101 bits (215), Expect = 7e-21
Identities = 45/69 (65%)
 Frame = +2 / +1
          GLLRANLTTMLTWSGRGFLGPLLPVGSQGIIVEPIDEILPTTPISEQKGGKPEPSAMPQP 181
Query: 2
           G+L + ML W G +GP P+ IVEP DEILPTTPISEQKGGKPEP AMPOP
Sbjct: 538 GVLGIKVKIMLPWDPTGKIGPKKPLPDHVSIVEPKDEILPTTPISEQKGGKPEPPAMPQP 717
Query: 182 VPTA*QVLL 208
           VPTA*Q LL
Sbjct: 718 VPTA*QGLL 744
Score = 100 bits (213), Expect = 1e-20
Identities = 36/39 (92%)
 Frame = -1 / -1
Query: 209 QGEPVMLWELAGAWQKALASHPSVLRWGWWAVSHLWVPQ 93
           QG+PVMLW LAGAWQ ALASHPSVLRWGWWAVSHLWVPQ
Sbjct: 745 QGDPVMLWGLAGAWQAALASHPSVLRWGWWAVSHLWVPQ 629
Score = 100 bits (213), Expect = 1e-20
Identities = 36/39 (92%)
 Frame = -2 / -2
Query: 208 KENLLCCGNWLGHGRRLWLPTLLF*DGGGGQYLIYGFHN 92
           KE LLCCG+WLGHGRRLWLPTLLF*DGGGGQYLI+GFHN
Sbjct: 744 KETLLCCGDWLGHGRRLWLPTLLF*DGGGGQYLIFGFHN 628
Score = 99.1 bits (210), Expect = 4e-20
Identities = 37/42 (88%)
 Frame = +1 / +3
Query: 82 PGHHCGTHR*DTAHHPHLRTEGWEARAFCHAPASSHSITGSP 207
           P HCGT R*DTAHHPHLRTEGWEARA CHAPAS HSITGSP
Sbjct: 618 PREHCGTQR*DTAHHPHLRTEGWEARAACHAPASPHSITGSP 743
Score = 93.2 bits (197), Expect = 2e-18
Identities = 35/40 (87%)
 Frame = +3 / +2
```

->Blast Result

Page 3 of 4

18

```
Query: 90 SLWNP*MRYCPPPPSQNRRVGSQSLLPCPSQFPQHNRFSL 209
           +LWNP MRYCPPPPSQNRRVGSQS LPCPSQ PQHNR SL
Sbjct: 626 ALWNPKMRYCPPPPSQNRRVGSQSRLPCPSQSPQHNRVSL 745
Score = 56.5 bits (117), Expect = 2e-07
Identities = 20/23 (86%)
 Frame = -3 / +1
Query: 93 MMPWDPTGNRGPKKPLPDHVSIV 25
           M+PWDPTG GPKKPLPDHVSIV
Sbjct: 565 MLPWDPTGKIGPKKPLPDHVSIV 633
Score = 55.6 bits (115), Expect = 5e-07
Identities = 20/25 (80%)
 Frame = +2 / -3
          TTMLTWSGRGFLGPLLPVGSQGIIV 97
Query: 23
           +TMLTWSGRGFLGP+LPVGSQG ++
Sbjct: 635 STMLTWSGRGFLGPILPVGSQGSMI 561
Score = 55.1 bits (114), Expect = 6e-07
Identities = 20/24 (83%)
 Frame = +1 / -2
Query: 22 YHNAHVVRQGLLRAPVTSWVPGHH 93
           +HNAHVVRQGLLRA +TSWVPG H
Sbjct: 636 FHNAHVVRQGLLRANLTSWVPGQH 565
Score = 51.9 bits (107), Expect = 6e-06
Identities = 21/27 (77%)
 Frame = -2 / +3
Query: 103 GFHNDALGPNW*QGP*EAPA*PREHCG 23
           G + ALGPNW* P*EAPA*PREHCG
Sbjct: 555 GEDHAALGPNW*DWP*EAPA*PREHCG 635
Score = 51.5 bits (106), Expect = 8e-06
Identities = 22/29 (75%)
 Frame = +3 / -1
Query: 21 LPQCSRGQAGAS*GPCYQLGPRASLWNP* 107
           +PQCSRGQAGAS*G YQLGPRA+ +P*
Sbjct: 637 VPQCSRGQAGAS*GQSYQLGPRAA*SSP* 551
Score = 49.6 bits (102), Expect = 3e-05
Identities = 20/22 (90%)
 Frame = -1 / +2
```

Page 4 of 4

Query: 89 CPGTQLVTGALRSPCLTT*ALW 24

CPGTQLV ALRSPCLTT*ALW

Sbjct: 569 CPGTQLVRLALRSPCLTT*ALW 634

CPU time:

0.10 user secs.

0.01 sys. secs

0.11 total secs.

Lambda K

0.318 0.135 0.401

Matrix: BLOSUM62

Number of Hits to DB: 1171 Number of Sequences: 0

Number of extensions: 38

Number of successful extensions: 20 Number of sequences better than 10.0: 1

length of database: 1,668,972,645

effective HSP length: 51

effective length of database: 1,261,711,380 effective search space used: 22710804840 frameshift window, decay const: 50, 0.1

T: 13 A: 40

X1: 16 (7.3 bits) X2: 109 (49.9 bits) S1: 41 (21.7 bits)



Blast 2 S quences results

PubMed

Entrez

BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION TBLASTX 2.2.2 [Dec-14-2001]

Match: 0 Mismatch: 0	gap open: 11 gap extension:	1
x_dropoff: 50 expect: 10.00	wordsize: 3 Filter 7	Nign
Sequence 1 lcl seq_1		Length 300 (1 300)
Sequence 2 gi <u>397648</u> Mus n	nusculus B6D2F1 clone 2C#4 mR	RNA. Length 962 (1 962)
	2	
		THE STATE OF STATE OF STATE OF
		
		99
		
<u> </u>		
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		1

NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

Score = 154 bits (330), Expect = 1e-35
Identities = 58/70 (82%)
Frame = +2 / +1

Page 2 of 5

```
Query: 89 ERDKNQSSSKRKVEQFWRFYSHMVRPGDLTGHSDFHLFKEGIKPMWEDDANKNGGKWIIR 268
                                                                                31
           E++ Q +
                       VEQFW+FYSHMVRPGDLTGHSDFHLFKEGIKPMWEDD NKNGGKWIIR
Sbjct: 268 EQNIKQIGTFPSVEQFWKFYSHMVRPGDLTGHSDFHLFKEGIKPMWEDDPNKNGGKWIIR 447
Query: 269 LRKGLASRCW 298
           LRKGLASRCW
Sbjct: 448 LRKGLASRCW 477
Score = 133 bits (286), Expect = 3e-30
Identities = 54/59 (91%)
 Frame = -1 / -1
Query: 300 SQQREAKPFRSRIIHLPPFLFASSSHMGLIPSLKRWKSLWPVRSPGRTMWL*NLQNCST 124
           SOOREAKPFRSR+IHLPPFLF SSSH+GLIPSLKR KSLWPVRSPGRTMWL*N QNCST
Sbjct: 479 SQQREAKPFRSRMIHLPPFLFGSSSHIGLIPSLKR*KSLWPVRSPGRTMWL*NFQNCST 303
Score = 112 bits (240), Expect = 7e-24
Identities = 47/58 (81%)
 Frame = -2 / -2
Query: 299 PSNGRPSPSAAE*STCHHFYLHHPPTWV*FLL*RDGSHCGLSGPQDVPCGYKTSRTAP 126
           PS+G+ SPS E*STC HFYL HPPT V* LL*RD SHCGLSGPQDVPCG KTSRTAP
Sbjct: 478 PSSGKLSPSGVE*STCPHFYLDHPPT*V*SLL*RDESHCGLSGPQDVPCGCKTSRTAP 305
Score = 110 bits (234), Expect = 5e-23
Identities = 45/58 (77%)
 Frame = -3 / -3
Query: 298 PATGGQALPQPNNPLATIFICIILPHGFNSFFEEMEVTVACQVPRTYHVAIKPPELLH 125
           PA G ALP+ N+PLA IFI IILPH FN FFEEM+VTVACQVPRTYHVA+K PELLH
Sbjct: 477 PAAGS*ALPESNDPLAPIFIWIILPHRFNPFFEEMKVTVACQVPRTYHVAVKLPELLH 304
Score = 109 bits (232), Expect = 9e-23
Identities = 47/58 (81%)
 Frame = +1 / +3
Query: 127 GAVLEVL*PHGTSWGPDRPQ*LPSLQRRN*THVGG*CK*KWWQVDYSAAEGLGLPLLG 300
           GAVLEVL PHGTSWGPDRPQ*L SLQRR+*T+VGG* K*KW QVD+S EGL PLLG
Sbjct: 306 GAVLEVLQPHGTSWGPDRPQ*LSSLQRRD*TYVGG*SK*KWGQVDHSTPEGLSFPLLG 479
Score = 102 \text{ bits } (217), \text{ Expect}(2) = 3e-33
Identities = 48/74 (64%)
 Frame = +3 / +2
```

Query: 78 RKKRNETRIRAVARERWSSSGGFIATWYVLGT*QATVTSISSKKELNPCGRMMQIKMVAS 257

Page 3 of 5

```
R+ + T R
                           WSSSG F ATWYVLGT*QATVT ISSKK LN CGRM+QIKM AS
Sbjct: 257 RRAMSRTSSRLAPFPLWSSSGSFTATWYVLGT*QATVTFISSKKGLNLCGRMIQIKMGAS 436
Query: 258 GLFGCGRAWPPVAG 299
           G F GRA P AG
Sbjct: 437 GSFDSGRA*LPAAG 478
Score = 74.4 bits (156), Expect(2) = 6e-14
Identities = 26/30 (86%)
 Frame = -2 / -3
Query: 92 VPFFPSHHLSVCCFLHSDHGPHCHHLSKRR 3
           V FFPSHHLSVCCFLHSDHG HCHHL +RR
Sbjct: 135 VLFFPSHHLSVCCFLHSDHGLHCHHLLRRR 46
Score = 74.4 bits (156), Expect(2) = 1e-12
Identities = 29/29 (100%)
Frame = +2 / +3
           FDALKDDDSGDHDQNEENSTQKDGEKEKT 88
Query: 2
           FDALKDDDSGDHDONEENSTOKDGEKEKT
Sbjct: 45 FDALKDDDSGDHDQNEENSTQKDGEKEKT 131
Score = 70.3 bits (147), Expect(2) = 7e-12
Identities = 29/30 (96%)
Frame = -1 / -2
Query: 90
          SVFSFSPSFCVLFSSF*SWSPLSSSFKASN 1
           +VFSFSPSFCVLFSSF*SWSPLSSSFKASN
Sbjct: 133 TVFSFSPSFCVLFSSF*SWSPLSSSFKASN 44
Score = 62.9 bits (131), Expect(2) = 3e-33
Identities = 27/31 (87%)
Frame = +1 / +2
          VRRFER**QWGP*SE*RKQHTERW*EGKNGT 93
Query: 1
           VRR +R**QW P*SE*RKQHTERW*EGKN T
Sbjct: 44 VRRLKR**QWRP*SE*RKQHTERW*EGKNST 136
Score = 58.3 bits (121), Expect = 2e-07
Identities = 26/41 (63%)
 Frame = +3 / +1
          STL*KMMTVGTMIRMKKTAHRKMVRRKKRNETRIRAVARER 125
Query: 3
           ST *KMMTV TMIRMKKTAHRKMVRRKK+
Sbjct: 46 STP*KMMTVETMIRMKKTAHRKMVRRKKQYRDKSQSSGKRK 168
```

```
Score = 57.4 bits (119), Expect = 4e-07
Identities = 26/34 (76%)
 Frame = -3 / -1
Query: 103 ILVSFRFFLLTIFLCAVFFILIMVPTVIIFQSVE 2
           +L + FFLLTIFLCAVFFILIMV TVIIF VE
Sbjct: 146 LLSRYCFFLLTIFLCAVFFILIMVSTVIIF*GVE 45
Score = 25.8 bits (50), Expect (2) = 6e-14
Identities = 9/15 (60%)
 Frame = -2 / -2
Query: 125 PFSCYCSDSCLVPFF 81
           P SC+CS SCL F
Sbjct: 169 PSSCHCSGSCLGTVF 125
Score = 23.1 bits (44), Expect(2) = 7e-12
Identities = 11/15 (73%)
 Frame = -3 / -3
Query: 124 LSLATALILVSFRFF 80
           L LATAL LVS FF
Sbjct: 168 LPLATALALVSVLFF 124
Score = 22.6 bits (43), Expect(2) = 1e-12
Identities = 10/15 (66%)
 Frame = +3 / +2
Query: 81 KKRNETRIRAVARER 125
           K ETR RAVAR R
Sbjct: 125 KNSTETRARAVARGR 169
CPU time:
          0.09 user secs.
                                    0.03 sys. secs
                                                           0.12 total secs.
Lambda
           K
   0.318
           0.135 0.401
Matrix: BLOSUM62
Number of Hits to DB: 1323
Number of Sequences: 0
Number of extensions: 37
Number of successful extensions: 16
Number of sequences better than 10.0: 1
length of database: 1,668,972,645
effective HSP length: 54
effective length of database: 1,368,557,577
effective search space used: 61585090965
frameshift window, decay const: 50, 0.1
```

Page 5 of 5 · Blast Result

T: 13

A: 40 X1: 16 (7.3 bits) X2: 109 (49.9 bits) S1: 41 (21.7 bits)